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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,508	09/12/2005	Jonathan Alexander Terrett	2543-1-038PCT/US	2562

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
09/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,508	TERRETT, JONATHAN ALEXANDER	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 21, 2008 has been entered.

2. Claims 11 and 28-30 are currently under consideration.

Rejections/Objections Maintained

Information Disclosure Statement

3. Applicant states that herewith a hard paper copy of the voluminous WO 01/22920A2 since a CD copy is not acceptable.

The information in WO 01/22920A2 has not been considered, because no copy was filed with the response and no information disclosure statement was filed.

It is noted that an information disclosure statement must comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement

Additionally, it is noted that an information disclosure statement must comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 11 and 28-30 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement essentially for the reasons previously set forth in the Office Action of January 29, 2008, section 4, pages 2-4.

Applicant argues that 1. All the steps required to practice the claimed invention short of actual therapy are clearly and unquestionably enabled.

The Examiner acknowledges that the specification teaches techniques for:

- the production of antibodies that bind to an antigen immunospecifically,
- methods of selecting antibodies for therapeutic use, and
- antibody-drug conjugation techniques

but then continues that the specification must contain the manner for making and using the invention. In particular, according to the Examiner, screening assays do not enable the claimed invention (citing, University of Rochester v. G.D. Searle 358 F.3d. 916, Fed. Cir., 2004) because they are merely a wish for a **chemical** invention [emphasis added]. Applicants argue that

current claim 11 is directed to a method of treating beast, lung and/or pancreatic cancer employing a monoclonal, chimeric, humanized or completely human antibody that specifically binds to the protein NKCC 1. Claim 28 depends on claim11 and is limited to where the antibody is a conjugate with certain chemical entities.

Applicant argues that Example 3 in the specification provides details of immunohistochemistry performed on breast cancer, pancreatic cancer and lung cancer tissue. The Examiner is respectfully reminded that immunohistochemistry staining employs an antibody conjugated to a chemical stain. When the antibody binds to a protein to which it is specific (in the instant invention, NKCC1), the relevant tissue is stained. Example 3 indicates that NKCC 1 immunostaining was seen in breast cancer tissue and it was clearly apparent that NKCC 1 is specifically and highly expressed in ductal carcinoma cells of the breast cancer tissue (compared with adjacent breast tissue). Of course all breast cancers are not of the same source or type, and out of 55 samples, 5 samples did not show staining. However, this is to be expected in the field. For example, in known breast cancer adjuvant therapies such as tamoxifen, certain patients are more suitable for treatment with the product than others. The most suitable cancers for treatment are those with estrogen receptors on the surface of their cells, termed 'estrogen-receptor-positive' (ER-positive). This does not reflect negatively upon the value of the therapy. In a separate example Her-2/neu expressing breast cancer is suitable for treatment with the pharmaceutical product Herceptin.

Applicant argues that Example 3 further teaches that increased staining of sections for NKCC 1 was seen in both lung and pancreatic tissue sections in comparison to adjacent control

sections. Thus, Example 3 provides evidence of the increased expression of the protein in the cancerous tissue and the ability of antibodies specific to NKCC 1 to bind to the protein in tissue.

Applicant argues that methods for making, screening and administering antibodies were routine in the art at the time the instant application was filed, and the association between the specific diseases is taught in the instant specification as filed. Yet, the Examiner maintains the rejection that the present specification does not teach how to make and use the invention as claimed, relying upon the decision of the Federal Circuit in University of Rochester v. G.D. Searle, supra.

Applicant's arguments have been considered, but have not been found persuasive. Although one of skill in the art could screen for antibodies that bind to SEQ ID NO: 1, the ability to identify an antibody that binds to its antigen is not a predictable indicator of its other activities, such as therapeutic efficacy. In particular Young et al. (US Pat. App. Pub 2004/0258693, Dec. 23, 2004) teaches that monoclonal antibody 7BD-33-11A binds to multiple cell lines, but only induced cytotoxicity in a small subset of those cells to which it bound, see Table 1 and 2 and para. 0100-0102. Additionally, Young et al. (US Patent Application Pub. 2004/0197328, October 7, 2004) teaches that monoclonal antibody 11BD-2E11-2 binds to MDA-MB-231 cells, but is not cytotoxic towards them, see para 0100-0104 and Tables 2 and 3. Furthermore, Young et al. (US Patent Application Pub. 2004/0197328, October 7, 2004) teach that while monoclonal antibody 11BD-2E11-2, which recognizes Melanoma-associated chondroitin sulfate proteoglycan (MCSP), is effective for treatment of breast and ovarian tumors (see examples 7 and 8), other monoclonal antibodies that also recognize MCSP, such as 9.2.27 and 225.28S, were ineffective as therapeutic antibodies, see para. 0014-0019. Thus even for

monoclonal antibodies that recognize the same protein, it cannot be predicted if the antibody will have the same activity towards cells expressing the targeted antigen. Thus, given the above and given that no antibody to SEQ ID NO: 1 has been shown to treat breast, lung, and/or pancreatic cancer; one of skill in the art could not predictably make and or use the claimed method without undue experimentation.

Furthermore, White et al. (2001, Ann. Rev. Med., 2001, 52:125-145), teach that, for a successful targeting and immunotherapy, besides specificity of the antibody for the antigen, other prosperities of the antigen should be considered including the following: (1) the antigen should be present on all or near all of the malignant cells to allow effective targeting and to prevent a subpopulation of antigen-negative cells from proliferating; and (2) whether antigens are shed, modulated, or internalized influences the effectiveness of the administered immunotherapy (i.e. the antibody) (p.126, 2nd para.). Given that the specification teaches that NKCC1/SEQ ID NO: 1 is expressed in the basolateral membrane of secretory epithelia (see page 1-lines 41-42), which would be away from the exposed apical surface of the cells (see Lodish et al. (Molecular Cell Biology, 2000, Figure 15-23), one of skill in the art would not predictably expect that NKCC1/SEQ ID NO: 1 could be effectively targeted by an antibody given that proteins expressed on the basolateral membrane are separated from the exposed apical membrane by tight junctions, see Lodish et al. (Molecular Cell Biology, 2000, Figure 15-23). Thus, given the location of NKCC1/SEQ ID NO: 1 in the cell membrane, it would not be expected that one could even predictably screen for antibodies to NKCC1/SEQ ID NO: 1 that would treat breast, lung, and/or pancreatic cancer

In addition, anti-tumor antibodies must accomplish several tasks to be effective. They must be delivered into the circulation that supplies the cancer and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. Also, the target cell must not have an alternate means of survival despite action at the proper site for the antibody. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The antibody may be inactivated *in vivo* before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half-life of the antibody. In addition, the antibody may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where it has no effect, circulation into the target area may be insufficient to carry the antibody and a large enough local concentration may not be established.

Thus, given the lack of a predictable correlation between antigen binding and anti-cancer activity of an antibody, given the basolateral expression of SEQ ID NO: 1/ NKCC1 that would predictably hinder any antibody from contacting SEQ ID NO:1 when administered *in vivo*, given the difficulties with antibody delivery, and in the absence of evidence in an appropriate model that an antibody to SEQ ID NO: 1/ NKCC1 is effective for treatment of breast, lung, and/or pancreatic cancer, undue experimentation would be required for one of skill in the art to predictably make, use, or even screen for antibodies that will function to treat breast, lung, and/or pancreatic cancer.

Applicant argues that 2. The facts of the controlling case law cited are clearly distinguishable.

Applicant argues that the facts of University of Rochester v. G.D. Searle are distinguishable in many ways. The University of Rochester v. G.D. Searle related to reach through claims, i.e. claims to chemical compounds identified in a screening method. Applicants argue that the court concluded that, as a matter of law, the patent at issue was invalid because a required compound was not disclosed and there was no pre-existing awareness in the art of such a compound exhibiting the claimed activity. Applicant submits that an important factor in the case is that it was not known how to make a selective COX-2 inhibitor when the application was filed. That is, in the University of Rochester v. G.D. Searle situation, knowing what the target receptor was provided little assistance to a skilled person to design a new chemical entity that that modulated the activity of the receptor.

The facts of the present invention are distinguishable in several respects:

1. The pending claims are not reach through claims but rather claims relating to a method of treatment;

2. Antibodies to the target protein were known before the instant application was filed and are exemplified in the application as filed;

3. One of ordinary skill in the art is able to prepare and screen other antibodies by well known techniques;

4. Once one of ordinary skill in the art has the antigen, antibodies to the antibody can be prepared without undue experimentation because there is a functional relationship between the two;

5. In the instant application as filed, binding in certain cancerous tissue and lower levels of expression of the relevant protein in healthy tissue is shown; and

6. One of ordinary skill in the art could administer the antibodies in a method of treatment in light of the teachings of the instant specification without undue experimentation, for example by infusion or vaccination.

Applicant's arguments have been considered, but have not been found persuasive. Although one of skill in the art could make and/or screen for antibodies that bind to SEQ ID NO: 1/NKCC1, given the lack of a predictable correlation between antigen binding and anti-canter activity of an antibody, given the basolateral expression of SEQ ID NO: 1/ NKCC1 that would predictably hinder any antibody from contacting SEQ ID NO:1 when administered *in vivo*, given the difficulties with antibody delivery, and in the absence of evidence in an appropriate model that an antibody to SEQ ID NO: 1/ NKCC1 is effective for treatment of breast, lung, and/or pancreatic cancer, undue experimentation would be required for one of skill in the art to predictably make, use, or even screen for antibodies that will function to treat breast, lung, and/or pancreatic cancer for the reasons set forth above and previously.

Applicant argues that 3. Antibody technology is relatively predictable.

Applicant argues that the Examiner's comment that screening assays do not enable the claimed invention (citing, Rochester v Seale 358 F.3d. 916, FED Cir., 2204) because they are merely a wish for a chemical invention, are merely reflective of novel chemical entities. The Examiner's reasoning is not applicable to antibodies, which are a specific class of biological molecules.

Applicant argues that the teachings of the present specification meet the requirement of 35 U.S.C. § 112 as regards method of treatment claims. In particular, it has never been the law

that clinical data must be available to meet the enablement requirement of 35 U.S.C. § 112. Applicant respectfully reminds the Examiner that in Glaxo v. Teva (2004 WL 1875017 D. Del 2004), the court concluded that there is no requirement in the law for working examples. Thus the fact that there is no clinical data in the specification does not render a rejection under 35 U.S.C. §112 proper.

Applicant's arguments have been considered, but have not been found persuasive. Although working examples are not required, and the Examiner is not requiring clinical data, given the unpredictability in the art previously set forth and above, in the absence of evidence that the method will function as claimed, undue experimentation would be required to make and/or use the claimed method. Although antibodies that bound SEQ ID NO: 1 could be made, antibodies that bound SEQ ID NO: 1 and that would function in the claimed method of cancer treatment could not predictably be made for the reasons set forth above and previously, thus undue experimentation would be required to make and use the invention.

Applicant argues that the Examiner asserts that the development of novel cancer therapeutics is unpredictable and thus this results in a failure to meet the criteria set of 35 U.S.C. § 112. Applicant agrees that in some instances the development of novel cancer therapeutics is unpredictable. However, Applicant argues that antibodies are distinguishable from simple new chemical entities (i.e. compounds which are simply inhibitors). Applicant argues that much of the case law relates to such new chemical entities. Applicant argues that this distinction can be drawn in part due to the high specificity of antibodies to the target protein and the functional interrelation of an antibody and a target protein. Applicant argues that in support of this fact, Applicant submits two articles herewith, discussing the success rate of antibody pharmaceutical

products, Ziegelbauer et al., Journal of Commercial Biotechnology 14(1):65-72 (2008) and Reichert et al., Drug Discovery 3:383 (2004). In particular Zeigelbauer et al. teach as follows:

> "Therapeutic antibodies have a high drug approval success rate once they reach clinical testing (29 percent for chimeric antibodies, 25 per cent for humanized antibodies compared to a success rate of approximately 11 per cent for small molecules), In addition, much of the development and clinical experience that is gained from the generation and optimization of one antibody product can be readily applied to subsequent therapeutic antibodies, diminishing some of the development, manufacturing, and clinical risks that are intrinsic to drug development.
> Owing to their exquisite specificity and ability to affect unique biological functions, monoclonal antibodies have the potential to provide a continued source of effective, safe, and reliable therapies. The introduction of such new therapies will benefit patients having a variety of debilitating diseases that otherwise respond poorly to alternate approaches. Based on the impact of the successful discovery of novel antibody functions on the current portfolio of antibody drugs, it is likely that the ability to continue to engineer novel functionalities by using new antibody formats will drive the expansion of the antibody drug market in the future."

Applicant argues that biological type products are much more likely (perhaps 4 or 5 times more likely) to be commercialized than a new chemical entity. Applicant submits that this in part is due to the specificity of antibodies in a biological context. Thus, relatively speaking Applicant submits that the unpredictability in the field under consideration is lower (perhaps significantly lower) than in other therapeutic fields.

Applicant's arguments have been considered, but have not been found persuasive. First it is noted that Ziegelbauer et al., Journal of Commercial Biotechnology 14(1):65-72 (2008) and Reichert et al., Drug Discovery 3:383 (2004) were not submitted with the response filed July 21, 2008, thus their relevance to enablement of the claimed method cannot be fully assessed. Although Zeigelbauer et al. argues that antibodies have a high drug approval rate once they reach clinical trials and Applicant argues, without any supporting evidence, that biological type products are much more likely (perhaps 4 or 5 times more likely) to be commercialized than a

new chemical entity, no evidence has been provided that an antibody to SEQ ID NO: 1 will function to treat of breast, lung, and/or pancreatic cancer in any model. Although antibodies have high specificity to the target protein and one of skill in the art could make and/or screen for antibodies that bind to SEQ ID NO: 1/NKCC1, given the lack of a predictable correlation between antigen binding and anti-canter activity of an antibody, given the basolateral expression of SEQ ID NO: 1/ NKCC1 that would predictably hinder any antibody from contacting SEQ ID NO:1 when administered *in vivo*, given the difficulties with antibody delivery, and in the absence of evidence in an appropriate model that an antibody to SEQ ID NO: 1/ NKCC1 is effective for treatment of breast, lung, and/or pancreatic cancer, undue experimentation would be required for one of skill in the art to predictably make, use, or even screen for antibodies that will function to treat breast, lung, and/or pancreatic cancer for the reasons set forth above and previously.

Applicant argues that 4. The USPTO guidelines for determining whether a specification is enabling for the claimed invention recognize that the specific facts and the state of the art must be considered in each instance such that no absolute rule exists.

Applicant respectfully directs the Examiner to USPTO educational materials provided in a presentation by Jean Witz http://www.cabic.con:ffbcp/031208/JWitz ECTT.ppt, a copy of which is enclosed. The USPTO educational materials indicate that:

That the amount of guidance or direction required to enable an invention is inversely proportional to the amount of knowledge in the art (and we know the skilled person in the biotech field is highly skilled);

• All the evidence must be weighed up by the Examiner;

• There are no rules per se (i.e., that apply unilaterally across the board); and

• The analysis should be performed on a case-by-case basis.

Applicant argues that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided, that there must be a reason to doubt the objective truth of the statements contained in the specification, that references should be supplied if possible to support a *prima facie* case of lack of enablement, and that specific technical reasons (to support a prima facie case of lack of enablement) are always required. Applicant argues that that the Examiner has failed to establish such a reasonable basis to question the enablement provided. Applicant argues that the Examiner has not established specific technical reasons to support the allegation that the specification does not enable the methods of treatment claimed. Applicant argues that still further, the Examiner has provided no references supporting such an allegation.

Applicant's arguments have been considered, but have not been found persuasive because the Examiner has supplied several references and technical reasons, see the Office Action of June 27, 2007, section 8, pages 3-10, and is supplying additional references and reasons to support a *prima facie* case of lack of enablement in this case. Thus, for the reasons previously set forth and above, the Examiner has established a *prima facie* case to support the argument that the specification does not enable the methods of treatment claimed. Additionally it is noted that a copy of presentation by Jean Witz was not enclosed in the response filed and the link provided was not active.

Applicant argues the following points:

• The present claims are not directed to a **cure** for the particular cancers but are claiming a method of treating certain cancers. Even established treatments including chemotherapy

and radiotherapy are not successful in one hundred percent of cases but are still valid methods of treatment.

• The claimed treatment may ultimately need to be used in combination with other treatments in a cocktail (this does not undermine the value of the present treatment as a component of same).

• Given antibodies have been shown to bind to the cancerous tissue expressing the relevant protein, the known antibodies could be used to at least some extent.

• Whether certain products make it to the market is sometimes a commercial decision based on a number of factors including the timing to the market and resources to support projects and therefore products that make it to market is not a good indication of unpredictability in the art.

Applicant argues that one of ordinary skill in the art could make and use a "method of treatment..." according to the present claims without undue experimentation.

Applicant's arguments have been considered, but have not been found persuasive. Although the claims are not drawn to cure and cancer treatments are known to be not one hundred percent effective, given the absence of any evidence in an appropriate model system that an antibody to SEQ ID NO: 1 alone or in combination with other treatments will function as claimed for the treatment of breast, lung, and/or pancreatic cancer, given the unpredictability in the art previously set forth and above, the claimed method is not enabled. Additionally, although antibodies bind to SEQ ID NO: 1 in tissue samples prepared for immunohistochemistry to allow for efficient antibody binding, given, as set forth above, that the binding of an antibody to antigen is not indicative of its therapeutic efficacy, thus the ability of antibody to bind the

antigen to which is directed does not predictably enable its use for cancer treatment. Furthermore, Examiner did not argue or require that the method make it to the market and/or be a commercial success in the market so this point is moot. Thus, for the reasons previously set forth and above, the method is not enabled and the rejections is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28-30 recite the limitation "the antibody" in claim 11. There is insufficient antecedent basis for this limitation in the claim. Specific enumeration of which antibody, the monoclonal, chimeric, humanized, or completely human antibody, is conjugated in claim 28 and from which antibody of these antibodies the fragments in claims 29 and 30 are made would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 11 and 28-30 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat. App. Pub. 2003/0148408 A1 (Frantz et al. October 19, 2001).

The claims are drawn to:

11. A method for the treatment of breast, lung and/or pancreatic cancer in a subject, which comprises administering to said subject a therapeutically effective amount of an antibody which is a monoclonal, chimeric, humanised or completely human antibody, wherein said antibody specifically binds to a NKCC1 polypeptide which consists of the amino acid sequence of SEQ ID NO: 1 as defined in claim 6.

28. The method according to claim 11, wherein the antibody is conjugated to a detectable substance, a therapeutic moiety, or a cytotoxic agent.

29. The method according to claim 11, wherein the antibody is a Fab fragment or F(ab')2 fragment.

30. The method according to claim 28, wherein the antibody is a Fab fragment or F(ab')2 fragment.

US Pat. App. Pub. 2003/0148408 A1 teaches therapeutically treating breast, lung and pancreatic cancer with therapeutically effective amounts of monoclonal , chimeric, or humanized antibodies or Fab or F(ab')2 fragments thereof to SEQ ID NO: 80, which is identical to SEQ ID NO:1 of the instant application, alone or conjugated to cytotoxic agents such as toxins and radioactive isotopes (which are detectable substances), see paragraphs 0210 to 0237 and 0572, Fig. 80 and Appendix 1.

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571)272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Helms Larry can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/
Examiner, Art Unit 1642
/P. J. R./

Appendix 1

Alignment of SEQ ID NO: 1 with SEQ ID NO: 80 of US Pat. App. Pub. 2003/0148408 A1.

```
US-10-241-220-80
; Sequence 80, Application US/10241220
; Publication No. US20030148408A1
; GENERAL INFORMATION:
;  APPLICANT: Frantz,Gretchen
;  APPLICANT:  Hillan,Kenneth J.
;  APPLICANT:  Phillips,Heidi
;  APPLICANT:  Polakis,Paul
;  APPLICANT:  Spencer,Susan
;  APPLICANT:  Williams,P.Mickey
;  APPLICANT:  Wu,Thomas
;  APPLICANT:  Zhang,Zemin
;  TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR THE DIAGNOSIS AND
;  TITLE OF INVENTION:  TREATMENT OF TUMOR
;  FILE REFERENCE: P5010R1-US
;  CURRENT APPLICATION NUMBER: US/10/241,220
;  CURRENT FILING DATE:  2002-12-13
;  NUMBER OF SEQ ID NOS: 120
; SEQ ID NO 80
;   LENGTH: 1212
;   TYPE: PRT
;   ORGANISM: Homo Sapien
US-10-241-220-80

  Query Match             100.0%;  Score 6227;  DB 4;  Length 1212;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 1212;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MEPRPTAPSSGAPGLAGVGETPSAAALAAARVELPGTAVPSVPEDAAPASRDGGGVRDEG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MEPRPTAPSSGAPGLAGVGETPSAAALAAARVELPGTAVPSVPEDAAPASRDGGGVRDEG 60

Qy         61 PAAAGDGLGRPLGPTPSQSRFQVDLVSENAGRAAAAAAAAAAAAAAAAGAGAGAKQTPADG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 PAAAGDGLGRPLGPTPSQSRFQVDLVSENAGRAAAAAAAAAAAAAAAAGAGAGAKQTPADG 120

Qy        121 EASGESEPAKGSEEAKGRFRVNFVDPAASSSAEDSLSDAAGVGVDGPNVSFQNGGDTVLS 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 EASGESEPAKGSEEAKGRFRVNFVDPAASSSAEDSLSDAAGVGVDGPNVSFQNGGDTVLS 180

Qy        181 EGSSLHSGGGGGSGHHQHYYYDTHTNTYYLRTFGHNTMDAVPRIDHYRHTAAQLGEKLLR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 EGSSLHSGGGGGSGHHQHYYYDTHTNTYYLRTFGHNTMDAVPRIDHYRHTAAQLGEKLLR 240

Qy        241 PSLAELHDELEKEPFEDGFANGEESTPTRDAVVTYTAESKGVVKFGWIKGVLVRCMLNIW 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 PSLAELHDELEKEPFEDGFANGEESTPTRDAVVTYTAESKGVVKFGWIKGVLVRCMLNIW 300

Qy        301 GVMLFIRLSWIVGQAGIGLSVLVIMMATVVTTITGLSTSAIATNGFVRGGGAYYLISRSL 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GVMLFIRLSWIVGQAGIGLSVLVIMMATVVTTITGLSTSAIATNGFVRGGGAYYLISRSL 360

Qy        361 GPEFGGAIGLIFAFANAVAVAMYVVGFAETVVELLKEHSILMIDEINDIRIIGAITVVIL 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GPEFGGAIGLIFAFANAVAVAMYVVGFAETVVELLKEHSILMIDEINDIRIIGAITVVIL 420
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Qy        421 LGISVAGMEWEAKAQIVLLVILLLAIGDFVIGTFIPLESKKPKGFFGYKSEIFNENFGPD 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 LGISVAGMEWEAKAQIVLLVILLLAIGDFVIGTFIPLESKKPKGFFGYKSEIFNENFGPD 480

Qy        481 FREEETFFSVFAIFFPAATGILAGANISGDLADPQSAIPKGTLLAILITTLVYVGIAVSV 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 FREEETFFSVFAIFFPAATGILAGANISGDLADPQSAIPKGTLLAILITTLVYVGIAVSV 540

Qy        541 GSCVVRDATGNVNDTIVTELTNCTSAACKLNFDFSSCESSPCSYGLMNNFQVMSMVSGFT 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 GSCVVRDATGNVNDTIVTELTNCTSAACKLNFDFSSCESSPCSYGLMNNFQVMSMVSGFT 600

Qy        601 PLISAGIFSATLSSALASLVSAPKIFQALCKDNIYPAFQMFAKGYGKNNEPLRGYILTFL 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 PLISAGIFSATLSSALASLVSAPKIFQALCKDNIYPAFQMFAKGYGKNNEPLRGYILTFL 660

Qy        661 IALGFILIAELNVIAPIISNFFLASYALINFSVFHASLAKSPGWRPAFKYYNMWISLLGA 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IALGFILIAELNVIAPIISNFFLASYALINFSVFHASLAKSPGWRPAFKYYNMWISLLGA 720

Qy        721 ILCCIVMFVINWWAALLTYVIVLGLYIYVTYKKPDVNWGSSTQALTYLNALQHSIRLSGV 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 ILCCIVMFVINWWAALLTYVIVLGLYIYVTYKKPDVNWGSSTQALTYLNALQHSIRLSGV 780

Qy        781 EDHVKNFRPQCLVMTGAPNSRPALLHLVHDFTKNVGLMICGHVHMGPRRQAMKEMSIDQA 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 EDHVKNFRPQCLVMTGAPNSRPALLHLVHDFTKNVGLMICGHVHMGPRRQAMKEMSIDQA 840

Qy        841 KYQRWLIKNKMKAFYAPVHADDLREGAQYLMQAAGLGRMKPNTLVLGFKKDWLQADMRDV 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 KYQRWLIKNKMKAFYAPVHADDLREGAQYLMQAAGLGRMKPNTLVLGFKKDWLQADMRDV 900

Qy        901 DMYINLFHDAFDIQYGVVVIRLKEGLDISHLQGQEELLSSQEKSPGTKDVVVSVEYSKKS 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 DMYINLFHDAFDIQYGVVVIRLKEGLDISHLQGQEELLSSQEKSPGTKDVVVSVEYSKKS 960

Qy        961 DLDTSKPLSEKPITHKVEEEDGKTATQPLLKKESKGPIVPLNVADQKLLEASTQFQKKQG 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 DLDTSKPLSEKPITHKVEEEDGKTATQPLLKKESKGPIVPLNVADQKLLEASTQFQKKQG 1020

Qy       1021 KNTIDVWWLFDDGGLTLLIPYLLTTKKKWKDCKIRVFIGGKINRIDHDRRAMATLLSKFR 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KNTIDVWWLFDDGGLTLLIPYLLTTKKKWKDCKIRVFIGGKINRIDHDRRAMATLLSKFR 1080

Qy       1081 IDFSDIMVLGDINTKPKKENIIAFEEIIEPYRLHEDDKEQDIADKMKEDEPWRITDNELE 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 IDFSDIMVLGDINTKPKKENIIAFEEIIEPYRLHEDDKEQDIADKMKEDEPWRITDNELE 1140

Qy       1141 LYKTKTYRQIRLNELLKEHSSTANIIVMSLPVARKGAVSSALYMAWLEALSKDLPPILLV 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 LYKTKTYRQIRLNELLKEHSSTANIIVMSLPVARKGAVSSALYMAWLEALSKDLPPILLV 1200

Qy       1201 RGNHQSVLTFYS 1212
              ||||||||||||
Db       1201 RGNHQSVLTFYS 1212
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